

Neural Events in the Reinforcement Contingency

Maria Teresa Araujo Silva, Fábio Leyser Gonçalves,
and Miriam Garcia-Mijares
University of São Paulo

When neural events are analyzed as stimuli and responses, functional relations among them and among overt stimuli and responses can be unveiled. The integration of neuroscience and the experimental analysis of behavior is beginning to provide empirical evidence of involvement of neural events in the three-term contingency relating discriminative stimuli, responses, and consequences. This paper is aimed at highlighting exemplar instances in the development of this issue. It has long been known that the electrical stimulation of certain cerebral areas can have a reinforcing function. Extraordinary technological advances in recent years show that neural activity can be selected by consequences. For example, the activity of *in vitro* isolated neurons that receive dopamine as a reinforcer functions as a cellular analogue of operant conditioning. The *in vivo* activity of populations of neurons of rats and monkeys can be recorded on an instant-to-instant basis and can then be used to move mechanical arms or track a target as a function of consequences. Neural stimulation acts as a discriminative stimulus for operant responses that are in turn maintained by neural consequences. Together with investigations on the molecular basis of classical conditioning, those studies are examples of possibilities that are being created for the study of behavior–environment interactions within the organism. More important, they show that, as an element in the three-term contingency, neural activity follows the same laws as other events.

Key words: neuroscience, behavioral analysis, operant conditioning, reinforcement contingency, neural activity

Among the several common misinterpretations of behavioral concepts is the black-box issue. Behaviorists are often assumed to treat the organism as a box, the contents of which are irrelevant in a behavioral analysis. A still amazingly widespread view of such issues holds that behaviorism considers external events as its exclusive object of study (e.g., Eysenck, 1984; Squire & Kandel, 2000). Yet, for a long time radical behaviorism has advanced the view that private events, “the world inside the skin,” can be understood in relation to behavior within the same framework as external events. With respect to accounts of behavior, inner events are denied any special status, because they share the same kinds of physical dimensions and are expected

to follow the same laws as public events. They are distinguished only by access. Because of this very difference, these events present special methodological difficulties in observation that render them difficult to subject to empirical study. However, “The line between public and private is not fixed. The boundary shifts with every new discovery of a technique for making private events public. ... The problem of privacy may, therefore, eventually be solved by technical advances” (Skinner, 1953, p. 282). We hope to document that new developments in neuroscience are shifting the boundary between public and private worlds.

In the intricate picture that is emerging from these advances, the world inside the skin is increasingly unveiled as part of the relation between environment and behavior. The dualistic view of an organism split between an inner self (or mind or brain) that is a self-determined commander and an external world is challenged. Skinner’s projections in 1974 are beginning to be documen-

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Address correspondence to the first author, Av. Prof. Mello Moraes, 1721 CEP 05508-020, São Paulo, SP, Brazil (e-mail: teresar@usp.br).






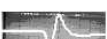


S^D	R	S^R	Example
			(a)
	 in vitro	dopamine	(b)
		water	(c)
visual		food	(d)
			(e)

Figure 1. Selected procedures in which neuronal responses and/or stimuli have been studied as part of a reinforcement contingency. S^D = discriminative stimulus; R = response; S^R = reinforcer. Icons indicate muscular or neural activity. Examples are from (a) Olds and Milner (1954); (b) Stein, Xue, and Belluzzi (1993); (c) Chapin, Moxon, Markowitz, and Nicolelis (1999); (d) Serruya, Hatsopoulos, Paninski, Fellows, and Donoghue (2002); (e) Talwar et al. (2002).

ted: “A small part of the universe is contained within the skin of each of us. There is no reason why it should have any special physical status because it lies within this boundary, and eventually we should have a complete account of it from anatomy and physiology” (p. 21). In fact, as pointed out by Catania, we “now know much more, and neuroscience and the science of behavior have each reached a point at which a modern synthesis holds great promise” (2000, p. 1). We will look at some recent experimental findings on conditioning and the nervous system, selected on the basis of their behavioral interest, even when the emphasis of the laboratories where they were conducted was on medical application. The focus of this paper is on the validity of behavioral laws regardless of stimulus type or response topography, and regardless of the private or public, internal or external, locus of the contingency elements. The

point will be made that observed neural events can function as elements in the behavior-analytic three-term contingency relating discriminative stimuli (S^D), responses (R), and reinforcers (S^R), thus extending the domain of behavior–environment interactions into the inner world within the skin.

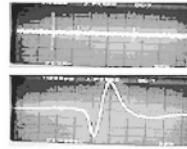
Figure 1 summarizes some paradigmatic experiments in which neural activity was treated explicitly as an element in the S^D –R– S^R contingency, so as to highlight representative instances of a functional analysis of neural events. We will discuss the role of neural activity as a reinforcing stimulus, when the reinforcer for a response stems from electrical stimulation of brain cells (Figure 1a); the role of dopamine in such reinforcing function (Figure 1b); the activity of neurons as a class of operant responses reinforced by consumatory stimuli (Figure 1c); the control of neural responses by external discrim-

OVERT OPERATION

1. R1 = bar-pressing



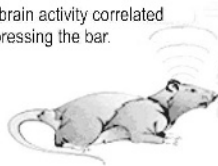
2. The system acquires neural activity...



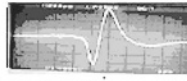
3. ...then its analysis identifies the brain patterns preceding R1

COVERT OPERATION

1. R2 = brain activity correlated with pressing the bar.



2. The system recognizes the signal



3. ... and delivers the water

Figure 2. In one of the experiments in Nicolelis' laboratory, rats were trained to press a bar to obtain water, and their neural signals were analyzed for patterns associated with pressing the bar. The system was programmed to detect those patterns, and the water dispenser was disconnected from the bar. Rats learned to activate the water dispenser exclusively by generating a neural code that met the reinforcement contingencies. (Illustration adapted from Jerry Schoendorf, Duke University Alumni Magazine, with permission.)

inative stimuli (Figure 1d); and the control of muscular responses by internal discriminative stimuli generated by cortical stimulation (Figure 1e). Each of these cases will be examined next.

NEURAL ACTIVITY AS A REINFORCER

The function of neural activity as a reinforcing stimulus was first revealed in the pioneering work of James Olds, who demonstrated that the electrical activity of some central neural structures had a reinforcing function (Olds & Milner, 1954). Briefly, the experiment consisted of electrical stimulation of certain areas of the brain contingent on a muscular response—a simple bar press (Figure 1a). Discriminative stimuli were not explicitly manipulated. These intracranial self-stimulation experiments, as they came to be called, opened the way to the investigation of specific brain areas that would yield positive reinforcing effects, as opposed to those that would function

as negative reinforcers. Since the 1960s, direct administration of chemicals into the brain was made contingent on operant responses, giving origin to the central self-administration model in studies of the neural substrates of reinforcement and disclosing the role of neurotransmitters in central reinforcement (Olds, Yuwiler, Olds, & Yun, 1964). It has been shown that animals will self-administer several drugs of abuse such as barbiturates, psychomotor stimulants, and opiates (McKim, 2003), establishing unquestionably the power of drugs as primary reinforcers. Although there may be microcircuit differences as shown, for example, by Carelli (Carelli, 2004; Carelli, Ijames, & Crumling, 2000), there is general agreement about a great deal of overlap in the central areas and pathways involved in the reinforcing action of abused substances and other reinforcers (Deadwyler, Haya-shizaki, Cheer, & Hampson, 2004; Kelley & Berridge, 2002; Wise, 2004). Thus, a collection of studies based on electrophysiological and pharma-

cological techniques began to build the case for neuroanatomical and neurochemical brain pathways mediating the occurrence of a variety of reinforcing events, derived from electrical and chemical reinforcers as well as from “natural” reinforcers such as food, water, and sex (Wise, 1998) and secondary reinforcers such as money (Knutson, Fong, Bennett, Adams, & Hommer, 2003). Presumably these neural systems evolved because differential sensitivity to natural reinforcers was important for survival and reproduction (Skinner, 1966); indeed, many of the molecular features of these systems are present in widely different species (Kelley & Berridge, 2002). The establishment of neural activity as a reinforcer led to models of the often designated “reinforcement system of the brain,” in which a prominent role is assigned to neurotransmitters as reinforcing agents.

The Role of Dopamine in Central Reinforcement

Models of central reinforcement hypothesize that reinforcement involves dopaminergic neurotransmission in the mesocorticolimbic system, as well as less well-known structures and transmitter systems (for reviews, see Kelley & Berridge, 2002; Koob & Bloom, 1988; Wise, 2002, 2004; Wise & Bozarth, 1987). The activation of dopamine D₂ receptors in the nucleus accumbens and the hippocampus is generally thought to be the final common pathway of a network of cellular and molecular events that take place in the brain when reinforcing stimuli occur contingent on behavior. Thus, a final dopamine release closes a cycle of multiple connections strengthened by reinforcement. The basis of the strengthening effect could be changes in synaptic efficacy between recently activated sensory and motor neurons in motor association areas (Donahoe & Palmer, 1994). These changes

would depend on the diffuse release of dopamine in these areas brought about by reinforcement and reinforcement-predicting stimuli (Phillips, Stuber, Heien, Wightman, & Carelli, 2003; Schultz, 2001). Brain dopamine seems thus to be crucial for the selection of response–reinforcer relations in the behavioral repertoire.

A SINGLE NEURON'S ACTIVITY AS THE UNIT OF RESPONSE

We turn now to the contingency depicted in Figure 1b, in which the activity of a single neuron is followed by dopamine. First, consider the following: A rat's bar press produces an electrical stimulation in the brain, the structures of the neurobiological network involved in this process begin to be disclosed, and dopamine is the key transmitter in this system. The question arises as to whether an effective experimental preparation could result from replacing the complex and continuous systemic responses of an animal with the activity of a single neuron as the unit of response, so that the reinforcement process could be seen at the level of the individual neuron. This problem prompted Stein and colleagues to arrange a model of a reinforcement contingency in which the electrical response of in vitro individual hippocampal neurons was followed by a dopamine microinjection (Stein, Xue, & Belluzzi, 1993, 1994). Stein et al. registered the electrical activity of single neurons in hippocampal slices maintained in a bath, and showed that the frequency of neuronal bursts increased as a function of dopamine microinjections contingent on a predetermined level of firing. Noncontingent injections, as well as injections of glutamate as a neurotransmitter control, did not produce any change. Extinction through suspension of dopamine delivery resulted in a reduction in bursting frequency. There was a proportional decrease in the strength of firing as

the interval between neuronal response and dopamine injection increased from 0 to 500 ms. Thus, a neuron maintained in vitro had provided a cellular analogue of basic principles of operant conditioning: the selection of a response as a function of a consequence, a decrease in strength with extinction, and the power of immediate reinforcement. Complex operant behavior would involve the collective action of a population of such neurons, the cellular and molecular basis of which was later proposed (Stein, 1997). Although the concept of a neural unit of response does not alter the investigation of ongoing operant behavior in an intact organism, it nevertheless adds another element linking different levels of analysis under the principle of selection by reinforcement.

A recent experiment by Byrne and his group of collaborators extended the in vitro reinforcement procedure to the sea snail *Aplysia* (Brembs, Lorenzetti, Reyes, Baxter, & Byrne, 2002). It had been known that swallowing food through buccal movements of a "biting" response stimulates this animal's esophageal nerve. Byrne and colleagues showed operant conditioning of the biting response in the freely behaving mollusk with a procedure similar to that used for rat intracranial stimulation: Dopamine-releasing electrical stimulation of the esophageal nerve was delivered contingent on the biting response. Response rate increased, whereas the biting frequency for animals that were noncontingently stimulated or not stimulated at all was not altered. For conditioned animals, increasing probability of biting behavior was correlated with increases in the activity of B51, a single buccal ganglia neuron known to be pivotal to the selection of buccal movements. Then, employing an in vitro system in another experiment, dopamine was applied to cultured B51 neurons contingent on

the exhibition of the firing pattern correlated with the biting behavior. As a result, the frequency of this pattern increased and cell properties underwent changes similar to those seen when biting had been reinforced, such as a decreased B51 burst threshold and increased input resistance. Although it is clear that a brain slice is not the living brain and a single neuron is not the whole organism, these analogues of operant conditioning have demonstrated the selective increase in the probability of emission of a response by a specific consequence, thus underscoring the functional similarity between such diverse topographies as those of neuronal and muscular response classes. The same behavioral laws that govern the relation between a muscular response and food, or even the dialogue between speaker and listener, have thus been shown to apply to a cellular response and a chemical or electrical reinforcer.

NEURAL PATTERNS AS AN OPERANT

A paradigmatic change in the process of extending behavioral study within the organism's skin was the demonstration that the activity of neurons can function as a class of operant responses reinforced by consummatory stimuli (Figure 1c). Nicolelis and his team of psychologists, neuroscientists, engineers, and information experts wondered whether a rat trained to press a bar for water would come to emit only the brain waves that had preceded the bar press if the reinforcement contingency were changed so that the overt bar press was no longer required to trigger the dispenser (Chapin, Moxon, Markowitz, & Nicolelis, 1999). Classic early experiments had shown operant reinforcement of a single cortical neuron's firing rate, with simultaneous suppression of muscle activity, when monkeys were presented with a stimulus that signaled a relevant conse-

quence contingent on bursts of cell activity (Fetz & Finocchio, 1971). Nicolelis' approach was based on the neurobiological principle that complex movement control is dependent on the collective activation of large distributed populations of neurons in the primary motor cortex.

A Rat Experiment

Rats were implanted with multiple electrodes in their primary motor cortex and were trained to bar press for water reinforcement (Figure 2). Animals pressed a spring-loaded lever to move a mechanical arm to collect a drop of water; the lever then had to be released to allow the arm to return with the water. Specially designed Teflon-insulated electrodes proved to be remarkably stable in this situation, providing simultaneous recording of the action potentials of up to 46 single neurons distributed across multiple cortical sites. The electrode array was connected via a cable to a data-acquisition unit linked to a computer system. Statistical signal-processing techniques were used to analyze the recorded brain signals. A neural network was designed to detect among incoming action potentials the particular patterns associated with the bar-pressing response. Permanent monitoring of premovement neuronal population activity allowed these flexible and interchangeable patterns to be continuously integrated and updated, thus yielding a moment-to-moment prediction of the bar-press movement—a “motor code” of the animal forelimb movement. These predictive neural signals could then be substituted for lever pressing as the operant behavior necessary to produce water.

In each experimental session, a trial began when the animal made a movement toward the lever using forearm flexion followed by arm flexion and finally paw extension; the forearm was then flexed to release the lever. These movement categories were de-

fined by electromiogram (EMG). The animals were allowed to work for about 5 min in the lever-pressing mode before being switched to the neural mode. The bar was then disconnected from the water dispenser, and the system was programmed to deliver water exclusively in response to the identified neural patterns that had predicted an effective lever press, whenever those occurred. In the lever-pressing mode, correlation between above-threshold lever movement and the preceding neuronal activity peak was high. However, when animals were shifted to the neural mode, that previously high correlation declined from $r = .81$ over the first 10 trials to an insignificant correlation for all subsequent sets of 10 trials. Notably, the animals were able to produce reinforcers on 60% to 100% of all trials in the neural mode. The premovement neuronal population signal resulted in the dispenser delivering a water drop without any movement above the threshold required by the lever-pressing mode contingency, or even without any forearm movement. Thus, the rats' brain waves, which had formerly preceded bar presses, now triggered the dispenser. The behavior of motor cortical neurons was the response element in the reinforcement contingency.

Monkeys

The basic design of the Chapin et al. (1999) experiment was improved and extended to owl monkeys, and a more complex movement was used instead of a bar press. The animals were implanted with arrays of about 100 electrodes distributed across several areas of their motor cortex (Wessberg et al., 2000). Seated on a special chair, the monkeys were trained in a discrete-trial task. As they watched two lights arranged horizontally on a display panel, the animals were required to move a joystick-like manipulandum to the left or right depending on whether the

left or right light was illuminated. Following each correct response, a small amount of fruit juice was delivered into a plastic tube close to the mouth through a computer-activated solenoid. Fiber-optic sensors attached to each monkey's wrist tracked the hand's trajectory. The action potentials generated during the task were sampled and integrated every 50 to 100 ms. As they were filtered, amplified, and analyzed by custom-made hardware, these neural signals revealed that the ensembles of cortical neurons predicted the position of each animal's hand a few hundred milliseconds before the action. Special software allowed the development of algorithms that translated such electrical activity into real-time predictions of the monkey's hand movements.

Once a neural output for hand trajectory was extracted, these cortically derived signals were used to command a computer directing a hidden robotic arm to mimic the monkey's arm movements (the robot movement would demonstrate the efficacy of the neural command). The brain activity of Belle, one of the monkeys, was then able to move one mechanical arm in the Duke University room next to where she was sitting in North Carolina, and another arm at an MIT laboratory in Massachusetts, with a small Internet transmission delay in the last case. As Nicolelis and Chapin (2002) have put it, "Belle's thought to receive her juice was a simple one, but a thought it was, and it commanded the outside world to achieve her very real goal" (p. 31). One is reminded of Skinner affirming that he saw "no reason why we should not also call the action of efferent nerves behavior if no muscular response is needed for reinforcement. This may occur in the thinking that retreats beyond the point at which muscular action can be detected" (Catania & Harnad, 1988, p. 485). Both in the rat and in the monkey, the electrical response of

a few neurons had been shown to produce a reinforcer and to be maintained by that reinforcer.

NEURAL ACTIVITY CONTROLLED BY EXTERNAL DISCRIMINATIVE STIMULI

Further experiments based on Nicolelis' paradigm explored explicit stimulus control. As sketched in Figure 1d, a contingency was set up in which neural activity was controlled by a visual stimulus. To begin, Donoghue and his collaborators taught a *Macaca mulatta* monkey to move a cursor toward a stimulus on a screen so as to hit the target and produce a reinforcer (Serruya, Hatsopoulos, Paninski, Fellows, & Donoghue, 2002). The animal could move a two-link manipulandum restricted to horizontal movement that controlled the position of the cursor (a green circle) on a video monitor. Hand movements, estimated at 50-ms intervals, produced an immediate change in the cursor's position. First the monkey was trained in a continuous tracking task to manually drive the cursor to fall within a randomly located target (i.e., a red circle, larger than the cursor). If the animal held the cursor within the target for 1 s, the target began to move smoothly and randomly on the computer screen. If the monkey followed the moving target, sustaining the feedback cursor within the target for 6 to 10 s, a juice reinforcer was delivered directly into the mouth via a computer-activated solenoid valve. The trial was aborted if the feedback cursor left the interior of the target during this time.

Once this performance was mastered, the moving target was replaced by a stationary one, which had to be reached within 20 s of its appearance. Each time the subject touched the target within the time constraint, a reinforcer was presented and the target jumped to a new random position, starting another discrete

trial. Because the cursor's trajectory could be seen on the screen, the subject had immediate response feedback. The activity from 7 to 30 cortical motor neurons was analyzed during the cursor's movement. A weighted sum of neural firing, taking into account the previous 1 s of hand activity, provided a reliable online reconstruction of the hand trajectory and was then used as the requirement for reinforcement (Serruya, Hatsopoulos, Fellows, Paninski, & Donoghue, 2003). After this neural-pattern-only training, the reinforcer was made contingent on either hand or neural responses. The monkey was immediately able to emit the necessary neural signal to control the cursor, making few, if any, target-directed arm movements. The median latencies to reach the target were similar whether the monkey had used hand or neural control, showing that neural control was nearly as effective as hand control. Thus, an external visual stimulus was shown to have a discriminative function for a neural response. Once again, the world inside the skin has been exposed and shown to follow the same laws relating externally observed responses and environmental events.

Simulating Proprioceptive Feedback

In the experiment described above, reaching the target provided visual feedback for the cursor response, and probably facilitated learning as a secondary reinforcer. Would animals learn to respond to a proprioceptive prosthetic feedback sensor eventually added to the experimental setup? Would it be "conscious" of its new arm? Would evidence of space allocation on the sensory cortex for this "artificial proprioceptor" be obtained? Prompted by these questions, Nicolelis wondered whether capabilities with a robotic arm could be extended by engineering a feedback arrangement—for example, by providing visual or tactile stimuli as

conditioned reinforcers in a contingency in which a brain response controlled the arm (Nicolelis & Chapin, 2002). Sensors that provided visual feedback on response force and direction were added to the experimental design in order to address these issues (Carmena et al., 2003).

A macaque monkey sat on a chair in front of a video display. While the collective activity of implanted frontoparietal neural ensembles was recorded, a computer analyzing the acquired data in real time was programmed to direct the movement of a cursor on the screen and of a mechanical arm equipped with a gripper, which the animal could not see. The animal was successively trained to perform three different tasks using a handheld pole equipped with a pressure transducer for measuring grasping force and an infrared marker to indicate hand position: a reaching task, a hand-gripping task, and a reach-and-grasp task. In the reaching task, a small disk (the cursor) and a large disk (the target) were presented to the animal. The manual response of moving the pole produced the consequence of changing the position of the cursor as well as of the robotic arm. Each trial began with the presentation of a target green disk (S^D) in a random location on the screen. The animal's task was to position the cursor inside the green disk. When this response requirement was met, the target changed colors (S^I), and the monkey received a juice reinforcer. The target had to be hit within 5 s or the trial would be computed as incorrect. In the hand-gripping task, the monkey was presented with the cursor inside two concentric circles. The ring formed by these two circles indicated the amount of force required, which changed every trial. Gripping the pole with the particular force instructed by the two circles (S^D) would move the hidden arm gripper and increase the cursor size (S^I), providing continuous feedback from the

gripping force. When the cursor size reached the required size, the monkey received a juice reinforcer. Thus, cursor position indicated the coordinates of the hidden robot hand, and cursor size provided feedback on force as measured by the grippers' sensors. The reach-and-grasp task was a combination of these two responses.

Monkeys were trained extensively in each one of these tasks, first on the pole-control mode, in which the reinforced response was the direct manipulation of the pole, then on the brain-control mode, in which manual pole responses had no consequence but the neural patterns that preceded the response changed the robotic arm position and force. Next, the pole itself was removed, and the robotic arm and cursor movements were made contingent exclusively on the brain responses. No wrist or biceps movements were detected by EMG recordings in this phase. The performance of the monkeys measured by time to complete a trial and percentage of correct trials improved with training in the three tasks, both in the pole and brain modes. Thus, the monkeys were able to make the robotic arm reach and grasp with their brain activity, and the progression of their performance suggested that the visual feedback on the gripper's movement and force functioned similarly to proprioceptive stimuli.

NEURAL ACTIVITY AS DISCRIMINATIVE STIMULUS

Neural activity produced by electrical stimulation entered the reinforcement contingency as discriminative and reinforcing stimuli for a muscular response in the so-called "robot rat" experiment, outlined in Figure 1e (Talwar et al., 2002). To begin, freely roaming rats carried on their backs a radio receiver and a power source able to transmit remote signals to very thin electrodes

implanted in their brains. An electrode placed in the medial forebrain bundle (MFB) of the brain provided the reinforcing stimulation. Electrodes were also implanted in the left or right somatosensory cortical region that normally processes signals from the rat's left and right whiskers, which were left intact. Stimulation on the right or left somatosensory cortical whisker-representation areas had no direct effect on behavior, but they generated discriminative stimuli for the animal turning either right or left. Training started with 10 sessions in a laboratory maze, in which MFB stimulation was delivered contingent on running forward and turning correctly whenever the "virtual touches" on the left or right cortical areas were presented. No prior training using direct mechanical stimulation of vibrissae was required. When correct responses reached a 100% criterion, the rats were moved to different spaces with no boundaries or fixed choice points. To induce new and complex responses, the researchers made use of both the reinforcing and the "priming" proactive effects of MFB stimulation (Gallistel, 1969). Thus, the MFB stimulation reinforced forward movement, and additional stimulation initiated further movement. On reaching an obstacle (e.g., a high step) a few MFB stimuli were sufficient to elicit a jump. The neural signals controlled a variety of responses in three-dimensional structures, first in the laboratory and later in an open space up to 500 m away from the stimulation source. Under extinction, stimulus control over behavior was lost. The responses induced in the so-called "ratbots" included climbing, jumping, passing through pipes, and crossing brightly lit open spaces. The orientation of these responses was signaled and reinforced by electrical stimuli that mimicked the covert events that presumably take place during the overt interaction between organism and environment. The whole contingency

was built around stimuli that came, as far as the animals were concerned, from within. Although this result has been described as “virtual learning” that “could make ratbots a new model for studying animal behaviour” (Clarke, 2002, p. 1), we might easily see it as actual learning in which ratbots demonstrate yet again a classic model for studying behavior.

NEURAL ANTECEDENTS OF NEURAL OPERANT BEHAVIOR

Research on neural operant behavior is now heading towards uncovering patterns that precede the neural motor command. A group of researchers led by Andersen moved the study of a neural motor response a step back (Musallam, Corneil, Greger, Scherberger, & Andersen, 2004). Monkeys were trained on the task of moving a cursor to reach a target discriminative stimulus on a screen to produce a juice reinforcer. However, the contingency specified an interval of approximately 1 s after stimulus presentation, during which trials were aborted if any hand movement occurred. During this period, neural activity away from the primary motor cortex was collected in a parietal area already known to be involved in directing hand-reaching movements. The activity thus extracted yielded an algorithm that in fact predicted the direction of movement. The algorithm was then used as a requirement for reinforcement on brain-controlled trials that were completed with success. Most remarkable, the prediction proved to be more accurate when the S^D was changed so as to indicate magnitude or quality of the reinforcer. The neural activity of the monkeys' brains indicated the direction of the movement to come, as well as the animals' preference and motivation in relation to the reinforcer, acting as a precursor of the covert and overt motor responses. The neural pattern told the experimenter, before any action,

which food and how much the monkeys preferred. Analyzed as behavior, these empirically observed “private” neural events may shed light on cognitive concepts such as intention or expectation.

CONCLUSION

An increasing number of researchers would agree that, in approaching neural events as elements in the reinforcement contingency, these events are not treated as underlying, mediating, or modulating behavioral events. Rather, they are seen as participating in functional relations defined by behavioral contingencies (Barnes-Holmes, 2003). As a first consequence of this perspective, the analysis of neural events as elements in the reinforcement contingency should facilitate a welcome interaction with neuroscientists, who may see the relevance of behavioral analysis more easily and be more inclined to consider its concepts and terms. Behavior analysts may be more often called in to undertake the appropriate analyses in order to lend behavioral significance to neuroscientific findings. Moreover, the just-overviewed findings in biobehavioral research point to the promise of expanding our present account of behavior and amplifying the range of practical applications.

Investigation of Inner Events

Before turning to the applied possibilities, a few illustrations of the expansion of the empirical domain of behavior are presented. The inclusion of the brain's activity into the expanded definition of behavior that emerges from the studies discussed may affect, mostly, the investigation of inner events. Experiments on classical and operant conditioning of *Aplysia* neurons, for example, may help in understanding the traditional dichotomy between these two paradigms of learning, investigating in detail similarities

and differences in their cellular and molecular underlying processes. Such experiments have already shown that both mechanisms are highly conserved across species (Brembs et al., 2002; Kandel, 2001), and they may eventually show that they share molecular processes in the cell nucleus. In a first approximation, an *in vitro* experimental setup that allows the observation of possible overlaps through the concurrent study of both operant and classical conditioning was developed (Brembs, Baxter, & Byrne, 2004). In that setup, the same response (buccal movements) can be elicited or reinforced by an antecedent or contingent unconditional stimulus (stimulation of esophageal nerve) and controlled by a conditional stimulus (stimulation of a sensory neuron). The *in vitro* analogue reproduced all of the cellular changes that previously were identified following *in vivo* classical and operant conditioning and led to the identification of several other neural changes related to learning. In an outlook to the future, the authors suggest that the above paradigm can be used in the investigation of questions such as “whether there are any operant components even in purely classical conditioning ... or whether classical and operant conditioning are merely two aspects of the same conditioning processes” (Brembs et al., 2004, p. 417).

Another instance comes from the important field of drug-addiction research. The conditioned response to several centrally acting drugs takes the opposite direction in relation to its unconditioned effect. For example, whereas the well-known unconditioned response to morphine is analgesia, the conditioned response to the morphine conditional stimulus is hyperalgesia. One interpretation of this apparent exception in classical conditioning assumes a compensatory role for the conditioned response, which would thus prepare the organism for the effects to come (Siegel,

1989). However, another interpretation is possible if one considers the neuronal response as the unconditioned response to the drug. In the above example, through negative feedback, a morphine injection leads to reduced neurotransmitter release from endorphin neurons, and it is the reduced endorphin output that becomes conditioned to the stimuli associated with the injection, resulting in hyperalgesia. If the behavioral analysis of these effects incorporates the neural event, the conditioned response to drug-related stimuli can no longer be seen as an exception to the usual similarity between conditioned and unconditioned responses (Donahoe & Palmer, 1994).

If brain events were studied as behavioral events, thoughts and feelings hitherto private might be adequately observed as neural activity. As technological advances reduce the space of the private world, progress in the research on that area might be expected. In the field of stimulus control, for instance, analysis at the neural level may be able to show directly the acquisition of stimulus–stimulus relations. It has already been reported that the matching-to-sample contingency leads to the selection of connections between cells in sensory association areas, in that these cells are selectively activated by the combination of the sample and comparison stimuli that signaled reinforcement (Erickson & Desimone, 1999; Sakai & Miyashita, 1991). The investigation of private events as neural events is also contributing to research on feelings. For example, after intravenous administration of reinforcing drugs such as cocaine, a clear correlation was demonstrated between self-reports of drug-induced private stimulation described as a “high” experience and increased dopaminergic function, assessed by dopamine D₂ receptor occupancy in position emission tomography (Volkow, Fowler, & Wang, 2002). This finding raises the possibility of

a role for brain dopamine in the discriminative function of the feeling that comes with reinforcement. As neuroimages begin to penetrate the world within the skin, we can envision an empirical basis for investigating covert events, pushing farther the dividing boundary between public and private.

Practical Applications

In the practical applications arena, Talwar and collaborators mentioned possible uses of the robot rat in searching the environment, as in looking for earthquake victims (Talwar et al., 2002). Other uses can be foreseen, if cultural contingencies call for the inspection of forbidden targets such as drugs or bombs. More appealing to compassion, however, are the perspectives of application of central operant activity in restoring neural function of paralyzed humans.

In fact, the operant brain activity of paralyzed patients is beginning to command the outside world. Amyotrophic lateral sclerosis victims were trained through operant procedures to select letters of the alphabet on a screen contingent on the production of specific electroencephalograph slow-cortical potentials (Birbaumer et al., 1999). A patient with locked-in syndrome has learned to control a computer cursor to produce synthetic speech and typing, using only the activity of primary motor cortex neurons collected through a few implanted electrodes (Kennedy, Bakay, Moore, Adams, & Goldwithe, 2000). The control of more complex movements using feedback from brain responses may be achieved through continuous adjustment of the mathematical algorithm that transforms neural activity into a control signal. Such adjustment is made possible with the population approach to neuronal conditioning.

The empirical study of neuronal population conditioning in humans has started. A team of researchers at

Duke University obtained acute recordings from subcortical neurons in Parkinson patients undergoing surgery. Simultaneously, the subjects performed a visual feedback hand-gripping force task on the screen, analogous to the monkey procedure already described. The researchers succeeded in extracting the neural parameters predictive of the patients' movements (Patil, Carmena, Nicolelis, & Turner, 2004). Despite being aware of the enormous challenges to be met in the practical implementation of brain-machine devices, the researchers considered that the neural signals they were able to extract seemed sufficient to predict movement and thus potentially command a robotic prosthesis, aided by sensory feedback from the robot's actions.

Recently, another step has been added in transferring the primate model to work with humans. In Donoghue's laboratory, when asked to imagine an action, a tetraplegic human's brain activity was isolated and used as the response requirement for reinforcement (Hochberg et al., 2006). Thus, a promising field of operant conditioning applications may be opened, with issues pertaining to imagination, motivation, stimulus control, and central feedback. Quoting the neurosurgeon Roy Bakay, "The demonstration of behavioral conditioning is essential to render feasible the principle of correlating multiple neuronal ensemble output into a behavioral task that can be used in human neuroprosthetics" (Patil et al., 2004, p. 37).

In summary, we conclude that environment-behavior interactions can be presently studied in a comprehensive behavior-analytic framework that incorporates advances in observation and manipulation of neural activity. We believe that the integration of neural activity as a component of the reinforcement contingency will contribute to the applied field of our science as well as to leading our knowledge to a point at which

“eventually a synthesis of the laws of behavior and of the nervous system may be achieved” (Skinner, 1938, p. 428).

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